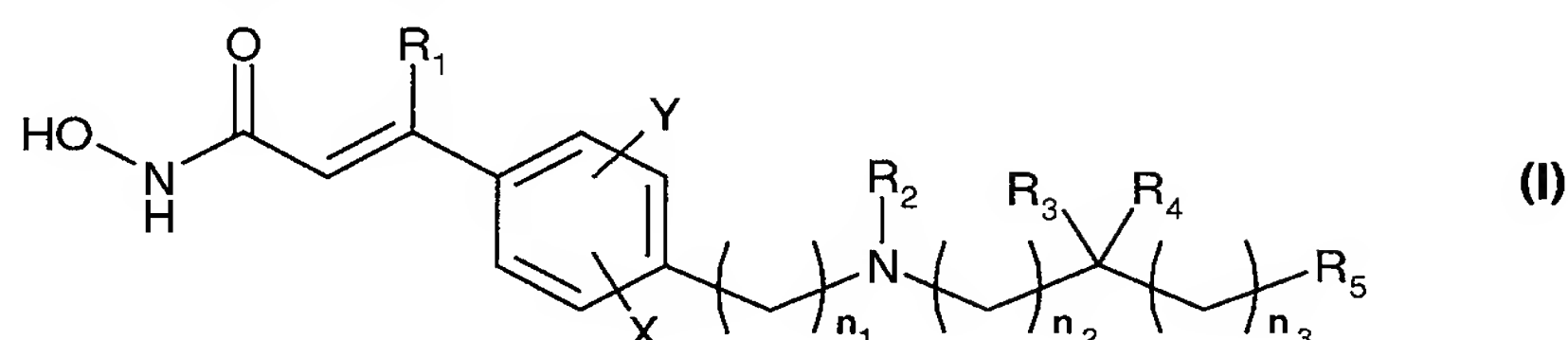


Amendments to the Claims:

Listing of the Claims:

1. (withdrawn) A combination comprising
- (a) death receptor ligand, and
- (b) a histone deacetylase inhibitor of formula (I)



wherein

R₁ is H; halo; or a straight-chain C₁-C₆alkyl, especially methyl, ethyl or *n*-propyl, which methyl, ethyl and *n*-propyl substituents are unsubstituted or substituted by one or more substituents described below for alkyl substituents;

R₂ is selected from H; C₁-C₁₀alkyl, preferably C₁-C₆alkyl, e.g., methyl, ethyl or -CH₂CH₂-OH; C₄-C₉cycloalkyl; C₄-C₉heterocycloalkyl; C₄-C₉heterocycloalkylalkyl; cycloalkylalkyl, e.g., cyclopropylmethyl; aryl; heteroaryl; arylalkyl, e.g., benzyl; heteroarylalkyl, e.g., pyridylmethyl; -(CH₂)_nC(O)R₆; -(CH₂)_nOC(O)R₆; amino acyl; HON-C(O)-CH=C(R₁)-aryl-alkyl-; and -(CH₂)_nR₇;

R₃ and R₄ are the same or different and, independently, H; C₁-C₆alkyl; acyl; or acylamino; or R₃ and R₄, together with the carbon to which they are bound, represent C=O, C=S or C=NR₈; or

R₂, together with the nitrogen to which it is bound, and R₃, together with the carbon to which it is bound, can form a C₄-C₉heterocycloalkyl; a heteroaryl; a polyheteroaryl; a non-aromatic polyheterocycle; or a mixed aryl and non-aryl polyheterocycle ring;

R₅ is selected from H; C₁-C₆alkyl; C₄-C₉cycloalkyl; C₄-C₉heterocycloalkyl; acyl; aryl; heteroaryl; arylalkyl, e.g., benzyl; heteroarylalkyl, e.g., pyridylmethyl; aromatic polycycles; non-aromatic polycycles; mixed aryl and non-aryl polycycles; polyheteroaryl; non-aromatic polyheterocycles; and mixed aryl and non-aryl polyheterocycles;

n, n₁, n₂ and n₃ are the same or different and independently selected from 0-6, when n₁ is 1-6, each carbon atom can be optionally and independently substituted with R₃ and/or R₄;

X and Y are the same or different and independently selected from H; halo; C₁-C₄alkyl, such as CH₃ and CF₃; NO₂; C(O)R₁; OR₉; SR₉; CN; and NR₁₀R₁₁;

R_6 is selected from H; C_1 - C_6 alkyl; C_4 - C_9 cycloalkyl; C_4 - C_9 heterocycloalkyl; cycloalkylalkyl, e.g., cyclopropylmethyl; aryl; heteroaryl; arylalkyl, e.g., benzyl and 2-phenylethenyl; heteroarylalkyl, e.g., pyridylmethyl; OR_{12} ; and $NR_{13}R_{14}$;
 R_7 is selected from OR_{15} ; SR_{15} ; $S(O)R_{16}$; SO_2R_{17} ; $NR_{13}R_{14}$; and $NR_{12}SO_2R_6$;
 R_8 is selected from H; OR_{15} ; $NR_{13}R_{14}$; C_1 - C_6 alkyl; C_4 - C_9 cycloalkyl; C_4 - C_9 heterocycloalkyl; aryl; heteroaryl; arylalkyl, e.g., benzyl; and heteroarylalkyl, e.g., pyridylmethyl;
 R_9 is selected from C_1 - C_4 alkyl, e.g., CH_3 and CF_3 ; $C(O)$ -alkyl, e.g., $C(O)CH_3$; and $C(O)CF_3$;
 R_{10} and R_{11} are the same or different and independently selected from H; C_1 - C_4 alkyl; and - $C(O)$ -alkyl;
 R_{12} is selected from H; C_1 - C_6 alkyl; C_4 - C_9 cycloalkyl; C_4 - C_9 heterocycloalkyl; C_4 - C_9 heterocycloalkylalkyl; aryl; mixed aryl and non-aryl polycycle; heteroaryl; arylalkyl, e.g., benzyl; and heteroarylalkyl, e.g., pyridylmethyl;
 R_{13} and R_{14} are the same or different and independently selected from H; C_1 - C_6 alkyl; C_4 - C_9 cycloalkyl; C_4 - C_9 heterocycloalkyl; aryl; heteroaryl; arylalkyl, e.g., benzyl; heteroarylalkyl, e.g., pyridylmethyl; amino acyl; or
 R_{13} and R_{14} , together with the nitrogen to which they are bound, are C_4 - C_9 heterocycloalkyl; heteroaryl; polyheteroaryl; non-aromatic polyheterocycle; or mixed aryl and non-aryl polyheterocycle;
 R_{15} is selected from H; C_1 - C_6 alkyl; C_4 - C_9 cycloalkyl; C_4 - C_9 heterocycloalkyl; aryl; heteroaryl; arylalkyl; heteroarylalkyl; and $(CH_2)_mZR_{12}$;
 R_{16} is selected from C_1 - C_6 alkyl; C_4 - C_9 cycloalkyl; C_4 - C_9 heterocycloalkyl; aryl; heteroaryl; polyheteroaryl; arylalkyl; heteroarylalkyl; and $(CH_2)_mZR_{12}$;
 R_{17} is selected from C_1 - C_6 alkyl; C_4 - C_9 cycloalkyl; C_4 - C_9 heterocycloalkyl; aryl; aromatic polycycles; heteroaryl; arylalkyl; heteroarylalkyl; polyheteroaryl and $NR_{13}R_{14}$;
 m is an integer selected from 0-6; and
 Z is selected from O; NR_{13} ; S; and $S(O)$,
 or a pharmaceutically acceptable salt thereof.

2. (original) A method for the prevention or treatment of proliferative diseases, in a mammal, which comprises treating the mammal with pharmaceutically effective amounts of a combination of:

- (a) death receptor ligand, and
- (b) a histone deacetylase inhibitor of formula (I) according to claim 1.

3. (withdrawn) The combination according to Claim 1, wherein the death receptor ligand is TRAIL, TRAIL/Apo-2L, TRAIL mimetics, agonistic antibodies, or other agents that can bind to

DR4 and DR5 triggering the activity of caspase-8 and apoptosis through the assembly of a cell-membrane associated multi-protein death inducing signaling complex (DISC).

4. (withdrawn) The combination of Claim 1, wherein the HDAl is selected from the group consisting of *N*-hydroxy-3-[4-[[2-(2-hydroxyethyl)[2-(1*H*-indol-3-yl)ethyl]-amino]methyl]phenyl]-2*E*-2-propenamide, *N*-hydroxy-3-[4-[[[2-(1*H*-indol-3-yl)ethyl]-amino]methyl]phenyl]-2*E*-2-propenamide and *N*-hydroxy-3-[4-[[[2-(2-methyl-1*H*-indol-3-yl)-ethyl]-amino]methyl]phenyl]-2*E*-2-propenamide, or a pharmaceutically acceptable salt thereof.

5. (withdrawn) The combination of Claim 1 for the prevention or treatment of leukemia.

6. (original) The method of Claim 2, wherein the mammal is a human.

7. (withdrawn) The combination of Claim 1 for the prevention or treatment of acute myeloid leukemia (AML).

8. (withdrawn) A combined preparation which comprises:

- (a) one or more unit dosage forms of a death receptor ligand; and
- (b) one or more unit dosage forms of a HDAl of formula (I) of Claim 1.

9. (withdrawn) The combined preparation according to Claim 8, wherein the death receptor ligand is TRAIL, TRAIL/Apo-2L, TRAIL mimetics, agonistic antibodies, or other agents that can bind to DR4 and DR5 triggering the activity of caspase-8 and apoptosis through the assembly of a cell-membrane associated multi-protein DISC.

10. (withdrawn) The combined preparation of Claim 9, wherein the histone deacetylase inhibitor is selected from the group consisting of *N*-hydroxy-3-[4-[[2-(2-hydroxyethyl)[2-(1*H*-indol-3-yl)ethyl]-amino]methyl]phenyl]-2*E*-2-propenamide, *N*-hydroxy-3-[4-[[[2-(1*H*-indol-3-yl)ethyl]-amino]methyl]phenyl]-2*E*-2-propenamide and *N*-hydroxy-3-[4-[[[2-(2-methyl-1*H*-indol-3-yl)-ethyl]-amino]methyl]phenyl]-2*E*-2-propenamide, or a pharmaceutically acceptable salt thereof.

11. (original) A method of treating or preventing premalignant proliferative diseases in a mammal which comprises treating the mammal with a combination of:

- (a) a pharmaceutically effective amount of a death receptor ligand; and
- (b) a pharmaceutically effective amount of *N*-hydroxy-3-[4-[[2-(2-hydroxyethyl)[2-(1*H*-indol-3-yl)ethyl]-amino]methyl]phenyl]-2*E*-2-propenamide, *N*-hydroxy-3-[4-[[[2-(1*H*-indol-3-yl)ethyl]-amino]methyl]phenyl]-2*E*-2-propenamide or *N*-hydroxy-3-[4-[[[2-(2-methyl-1*H*-

indol-3-yl)-ethyl]-amino]methyl]phenyl]-2*E*-2-propenamide; or a pharmaceutically effective salt thereof.

12. (original) The method according to Claim 11, wherein the death receptor ligand is TRAIL, TRAIL/Apo-2L, TRAIL mimetics, agonistic antibodies, or other agents that can bind to DR4 and DR5 triggering the activity of caspase-8 and apoptosis through the assembly of a cell-membrane associated multi-protein DISC.

13. (original) A method of treating or preventing proliferative diseases in a mammal which comprises treating the mammal with a combination of:

- (a) a pharmaceutically effective amount of a death receptor ligand; and
- (b) a pharmaceutically effective amount of an HDAI.

14. (withdrawn) A combined preparation which comprises:

- (a) one or more unit dosage forms of a death receptor ligand; and
- (b) one or more unit dosage forms of a HDAI.